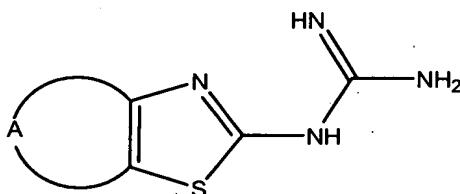


Claims

1. Use of guanidine derivatives of general formula

5



I

in which

A represents a chain of 3-6 optionally substituted C atoms, one of which can be

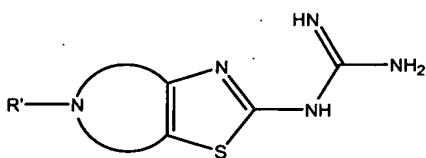
10 replaced by -N(R')- or -O-; and

R' represents hydrogen or a substitute;

the ring skeleton containing only the two double bonds of the thiazole component; of pharmaceutically applicable acid addition salts of basic compounds of formula I, pharmaceutically applicable salts of acid group-containing compounds of formula I with 15 bases, pharmaceutically applicable esters of hydroxy or carboxy group-containing compounds of formula I and hydrates or solvates thereof; as neuropeptide FF receptor antagonists or for the preparation of corresponding medicinal products.

20 2. Use according to claim 1 for the treatment of pain and hyperalgesia, withdrawal syndromes in the case of alcohol, psychotropic and nicotine dependences and for the improvement or elimination of these dependences, for the regulation of insulin secretion, food intake, memory functions, blood pressure, and of the electrolyte and energy balance and for the treatment of urinary incontinence or for the preparation of 25 corresponding medicinal products.

3. Use according to claim 1 or 2 of compounds of the general formula



III

in which R' means alkyl, alkanoyl, alkenyl, alkinyl, alkoxycarbonylalkyl,
 alkoxycarbonylaminoalkanoyl, alkylcarbamoyl, alkoxycarbonylalkylcarbamoyl,
 alkoxycarbonylalkylthiocarbamoyl, alkylthiocarbamoyl, mono- or disubstituted
 5 aminoalkanoyl, aryl, arylalkyl, arylalkoxycarbonyl, arylalkanoyl, arylcarbamoyl,
 alkoxyalkanoyl, alkylsulphonyl, arylthiocarbamoyl, aryloxycarbonylalkyl,
 aryloxycarbonylalkanoyl, aryloxycarbonylalkylcarbamoyl, aryloxycarbonylalkylthio-
 carbamoyl, arylsulphonyl, cycloalkyl, cycloalkanoyl, cycloalkylcarbamoyl,
 cycloalkylthiocarbamoyl, cycloalkylcarbonyl, cycloalkyloxycarbonylalkyl,
 10 cycloalkyloxycarbonylalkanoyl, cycloalkyloxycarbonylalkylcarbamoyl,
 cycloalkyloxycarbonylalkyl-thiocarbamoyl, heterarylalkyl, heterocyclalkyl,
 heterocyclalkoxycarbonylalkyl, heterocyclalkoxycarbonylalkanoyl,
 heterocyclalkoxycarbonylalkylcarbamoyl,
 heterocyclalkoxycarbonylalkylthiocarbamoyl, heteroaryloxycarbonylalkyl, hetero-
 15 aryloxycarbonylalkylcarbamoyl or heteroaryloxycarbonylalkylthiocarbamoyl.

4. Use according to claim 3, in which the ring skeleton contains a thiazolopyridine, thiazoloazepine or thiazolooxepane skeleton, which contains only the two double bonds of the thiazole component.

20

5. Use according to claim 4, in which the ring skeleton is a 5,6-dihydro-4H-cyclopentathiazole, 6,7-dihydro-4H-pyrano[4,3-d]thiazole, or 5,6,7,8-tetrahydro-4H-thiazolo[4,5-c]azepine skeleton.

25

6. Use according to one of claims 3-5, in which R' means methyl, ethyl, propyl, hexyl, 2,2-dimethylpropionyl, cyclopropylmethyl, 2-cyclohexylethyl, propinyl, ethyloxycarbonylethyl, benzyl, n-butyloxycarbonyl, *tert*-butyloxycarbonyl, benzyloxycarbonyl, 3-methyl-butyryl, pentanoyl, phenylacetyl, 2-propyl-pentanoyl, cyclopropanecarbonyl, isobutyryl, but-3-enoyl, 2-methoxy-acetyl, propane-2-sulphonyl,

butane-1-sulphonyl, methanesulphonyl, *tert*-butyloxycarbonyl-aminopropionyl or 4-dimethylamino-butyryl.

7. Use according to claim 1 or 2 of

5 2-guanidino-6,7-dihydro-4*H*-thiazolo[5,4-c]pyridine-5-carboxylic acid *tert*-butyl ester; N-(5-hexyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl)-guanidine; N-[5-(2-cyclohexyl-ethyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl]-guanidine; N-(5-ethyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl)-guanidine; 2-guanidino-6,7-dihydro-4*H*-thiazolo[5,4-c]pyridine-5-carboxylic acid butyl ester;

10 10 N-[5-(propane-2-sulphonyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl]-guanidine; N-(5-phenylacetyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl)-guanidine; 2-guanidino-6,7-dihydro-4*H*-thiazolo[5,4-c]pyridine-5-carboxylic acid benzyl ester; N-(5-pentanoyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl)-guanidine; 2-guanidino-6,7-dihydro-4*H*-thiazolo[5,4-c]pyridine-5-thiocarboxylic acid propyl

15 amide; N-[5-(2-propyl-pentanoyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl]-guanidine; N-(5-benzyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl)-guanidine; N-(5-prop-2-ynyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl)-guanidine; N-(5-cyclopropanecarbonyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl)-guanidine;

20 20 N-[5-(butane-1-sulphonyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl]-guanidine; N-(5-isobutyryl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl)-guanidine; N-[5-(2,2-dimethyl-propionyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl]-guanidine; 2-guanidino-6,7-dihydro-4*H*-thiazolo[5,4-c]pyridine-5-thiocarboxylic acid benzyl

25 amide; 2-guanidino-6,7-dihydro-4*H*-thiazolo[5,4-c]pyridine-5-carboxylic acid *tert*-butyl amide; N-(5-but-3-enoyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl)-guanidine; N-(5-benzyl-5,6,7,8-tetrahydro-4*H*-thiazolo[4,5-c]azepine-2-yl)-guanidine; 3-(2-guanidino-6,7-dihydro-4*H*-thiazolo[5,4-c]pyridine-5-yl)-propionic acid ethyl ester;

30 30 2-guanidino-6,7-dihydro-4*H*-thiazolo[5,4-c]pyridine-5-carboxylic acid pentyl amide; N-[5-(2-methoxy-acetyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl]-guanidine; N-(5-cyclopropylmethyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl)-guanidine;

N-(5-methanesulphonyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl)-guanidine;
N-[5-(3-methyl-butyryl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl]-guanidine;
2-guanidino-6,7-dihydro-4H-thiazolo[5,4-c]pyridine-5-thiocarboxylic acid-(2-methoxy-
1-methyl-ethyl)-amide;

5 2-guanidino-6,7-dihydro-4H-thiazolo[5,4-c]pyridine-5-carboxylic acid phenyl amide;
[3-(2-guanidino-6,7-dihydro-4H-thiazolo[5,4-c]pyridine-5-yl)-3-oxo-propyl]-carbamic
acid *tert*-butyl ester;

N-[5-(4-dimethylamino-butyryl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl]-
guanidine;

10 N-(5-propyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-yl)-guanidine; and
2-guanidino-6,7-dihydro-4H-thiazolo[5,4-c]pyridine-5-thiocarboxylic acid isopropyl
amide.

8. Compounds of Formula I defined in claim 1, in which A means a chain of 3-6
15 optionally substituted C atoms, one of which can be replaced by -O-, the ring skeleton
containing only the two double bonds of the thiazole component;
pharmaceutically applicable acid addition salts of basic compounds, pharmaceutically
applicable salts of acid group-containing compounds with bases, pharmaceutically
applicable esters of hydroxy or carboxy group-containing compounds as well as
20 hydrates or solvates thereof;

with the exception of

- N-(4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
- (2-guanidino-4,5,6,7-tetrahydro-benzothiazole-4-yl)-ethyl acetate ethyl ester;
- N-(4-hydroxymethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
- 25 - N-(4-tosyloxymethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
- N-(4-azidomethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
- N-(4-aminomethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine; and
- N-(6-acetylaminomethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine.

30 9. Compounds according to claim 8, in which, in chain A
- one of the C atoms carries one or two identical or different substituents; or
- several of the C atoms each carry one or two identical or different substituents.

10. Compounds according to claim 9, in which the substituent(s) are selected from alkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, aralkyl, alkoxycarbonyl, carboxamido, cyano or cyanolakyl groups and/or from polymethyl groups linked with one and the
5 same C atom.

11. Compounds according to claim 10, in which the substituent(s) is/are selected from

- methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, *sec*-butyl, *tert*-butyl, 1,1-dimethylpropyl, allyl and cyclohex-1-enyl groups; and/or
- phenyl, o-tolyl, m-tolyl, p-tolyl, 2-ethylphenyl, 3-fluorophenyl, 4-fluorophenyl, 4-chlorophenyl, 4-cyanophenyl, 4-benzoyloxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 3,4-dimethoxyphenyl, 3,4-methylenedioxyphenyl and to-3,5-trifluoromethylphenyl groups; and/or
- 15 - thiophene-2-yl and benzyl groups; and/or
- ethoxycarbonyl groups; and/or
- n-propylamino, benzylamino, N-methyl-N-phenethylamino, 3-methylbutylamino, phenylamino, N-butyl-N-ethylamino, di-n-propylamino, allylamino, piperidine-1- and morpholine-4-carbonyl groups; and/or
- 20 - cyano and cyanoethyl groups; and/or
- pentamethylene groups linked with one and the same C atom.

12. Compounds according to claim 11, in which there is located on one and the same C atom on the one hand a phenyl group and on the other hand an ethoxycarbonyl, cyano
25 or phenyl group.

13. *N*-(5-ethyl-5-methyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate;
N-(5,5-dimethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate;
30 *N*-(5,5-dimethyl-6-phenyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate;
N-(4-*tert*-butyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;

N-(6-isopropyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
N-(5,5,7-trimethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
N-(6,6-dimethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
N-(5-butyl-5,6,7,8-tetrahydro-4*H*-cycloheptathiazol-2-yl)-guanidine;

5 *N*-(4-ethyl-4-methyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
N-[6-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydro-benzothiazole-2-yl]-guanidine and its formate;
N-(5-butyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
N-(6-phenyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;

10 10 *N*-(5-methyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
N-(4-methyl-4-propyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
N-(6-propyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
N-(4-cyclohex-1-enyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate;
N-(4-*sec*-butyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate; and

15 15 *N*-(4-isobutyl-4-methyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine.

14. *N*-(6-*tert*-butyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
2-guanidino-6-phenyl-4,5,6,7-tetrahydro-benzothiazole-6-carboxylic acid ethyl ester and its formate;

20 20 *N*-[6-(1,1-dimethyl-propyl)-4,5,6,7-tetrahydro-benzothiazole-2-yl]-guanidine;
N-(7-methyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate;
N-[6-(3-methoxy-phenyl)-4,5,6,7-tetrahydro-benzothiazole-2-yl]-guanidine and its formate;
N-(6-thiophene-2-yl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate;

25 25 *N*-(5,5,7,7-tetramethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
N-[6-(4-fluorophenyl)-4,5,6,7-tetrahydro-benzothiazole-2-yl]-guanidine and its hydrobromide;
2-guanidino-4,5,6,7-tetrahydro-benzothiazole-6-carboxylic acid ethyl ester and its hydrobromide;

30 30 *N*-(4,4-dimethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
N-(4-methyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate;

N-(4,5,6,7-tetrahydro-benzothiazole-2-yl-4-spiro-cyclohexane)-guanidine and its formate;

N-(5,6,7,8-tetrahydro-4*H*-cycloheptathiazol-2-yl)-guanidine;

N-(4-allyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate;

5 *N*-(6-methyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;

N-[6-(3-fluorophenyl)-4,5,6,7-tetrahydro-benzothiazole-2-yl]-guanidine and its formate;

N-(6-cyano-6-phenyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its hydrobromide;

N-(4-phenyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate; and

10 *N*-(6,6-diphenyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate.

15. *N*-[6-(4-methoxy-phenyl)-4,5,6,7-tetrahydro-benzothiazole-2-yl]-guanidine and its hydrobromide;

N-(5-phenyl-5,6,7,8-tetrahydro-4*H*-cycloheptathiazol-2-yl)-guanidine and its hydrobromide;

15 *N*-(6,7-dihydro-4*H*-pyrano[4,3-d]thiazol-2-yl)-guanidine;

N-(6-benzo[1,3]dioxol-5-yl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate;

20 2-guanidino-4,5,6,7-tetrahydro-benzothiazole-6-carboxylic acid propyl amide and its formate;

N-[6-(4-cyanophenyl)-4,5,6,7-tetrahydro-benzothiazole-2-yl]-guanidine and its formate;

N-(4-benzyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate;

25 *N*-(5-methyl-5-phenyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate;

N-[6-(3,5-to-trifluoromethylphenyl)-4,5,6,7-tetrahydro-benzothiazole-2-yl]-guanidine and its formate;

30 *N*-(6-*o*-tolyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate;

N-(6-*m*-tolyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate;

N-[6-(2-ethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazole-2-yl]-guanidine and its formate;

N-[6-(4-chlorophenyl)-4,5,6,7-tetrahydro-benzothiazole-2-yl]-guanidine and its formate;

30 2-guanidino-4,5,6,7-tetrahydro-benzothiazole-4-carboxylic acid benzyl amide and its formate;

N-(5,6-dihydro-4*H*-cyclopentathiazol-2-yl)-guanidine;

N-[6-(4-benzyloxy-phenyl)-4,5,6,7-tetrahydro-benzothiazole-2-yl]-guanidine and its hydrobromide;

2-guanidino-4,5,6,7-tetrahydro-benzothiazole-4-carboxylic acid methyl phenethyl amide and its formate;

5 N-(6-phenyl-4,5,6,7-tetrahydro-benzothiazole-2-yl-4-spiro-cyclohexane)-guanidine and its hydrobromide;

N-(6-p-tolyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine and its formate

2-guanidino-4,5,6,7-tetrahydro-benzothiazole-4-carboxylic acid-(3-methyl-butyl)-amide and its formate; and

10 N-(4-*tert*-butyl-6-phenyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine.

16. 2-guanidino-4,5,6,7-tetrahydro-benzothiazole-6-carboxylic acid phenyl amide and its formate;

2-guanidino-4,5,6,7-tetrahydro-benzothiazole-4-carboxylic acid butyl ethyl amide and

15 its formate;

N-[4-(2-cyano-ethyl)-4,5,6,7-tetrahydro-benzothiazole-2-yl]-guanidine and its formate;

2-guanidino-4,5,6,7-tetrahydro-benzothiazole-4-carboxylic acid ethyl ester and its hydrobromide;

2-guanidino-4,5,6,7-tetrahydro-benzothiazole-4-carboxylic acid dipropyl amide and its

20 formate;

2-guanidino-4,5,6,7-tetrahydro-benzothiazole-4-carboxylic acid phenyl amide and its formate;

2-guanidino-4,5,6,7-tetrahydro-benzothiazole-6-carboxylic acid allyl amide and its formate;

25 2-guanidino-4,5,6,7-tetrahydro-benzothiazole-4-carboxylic acid propyl amide and its formate;

N-[4-(piperidine-1-carbonyl)-4,5,6,7-tetrahydro-benzothiazole-2-yl]-guanidine and its formate;

2-guanidino-4,5,6,7-tetrahydro-benzothiazole-4-carboxylic acid allyl amide and its

30 formate;

2-guanidino-4,5,6,7-tetrahydro-benzothiazole-6-carboxylic acid-(3-methyl-butyl)-amide and its formate;

N-[4-(morpholine-4-carbonyl)-4,5,6,7-tetrahydro-benzothiazole-2-yl]-guanidine and its formate; and

2-guanidino-4,5,6,7-tetrahydro-benzothiazole-4-carboxylic acid diisopropyl amide and its formate.

5

17. Compounds according to one of claims 8-16 for use as therapeutic active ingredients.

18. A medicinal product, containing a compound according to one of claims 8-16

10 and an inert carrier.

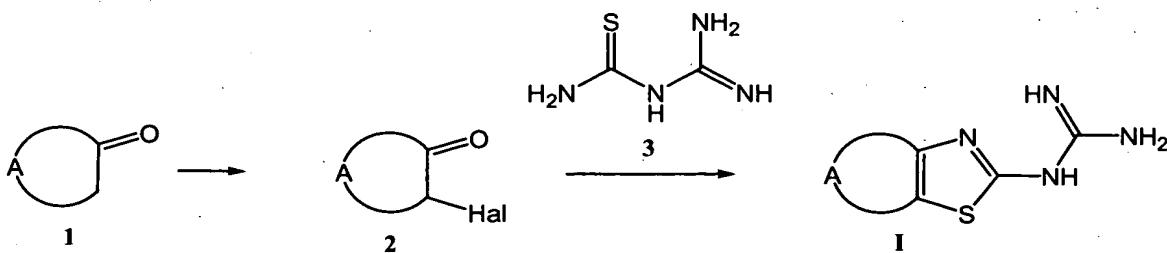
19. Use of compounds according to one of claims 8-16, according to claim 1 or 2.

20. Use of

15 - *N*-(4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
- (2-guanidino-4,5,6,7-tetrahydro-benzothiazole-4-yl)-ethyl acetate ethyl ester;
- *N*-(4-hydroxymethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
- *N*-(4-tosyloxymethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
- *N*-(4-azidomethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine;
20 - *N*-(4-aminomethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine; and
- *N*-(6-acetylaminomethyl-4,5,6,7-tetrahydro-benzothiazole-2-yl)-guanidine
according to claim 1 or 2.

21. Method for the preparation of compounds according to one of claims 8-16,

25 characterized in that a compound of the following Formula 1



is halogenated in α -position to form the carbonyl group, the obtained compound of the above Formula 2 is subjected to a cyclocondensation with 2-imino-4-thiobiuret of the above Formula 3 and optionally an obtained basic compound is converted into a

5 pharmaceutically applicable acid addition salt or an obtained compound, containing an acid group, into a pharmaceutically applicable salt with a base or an obtained, hydroxy- or carboxy group-containing, compound into a pharmaceutically applicable ester and optionally the obtained product into a hydrate or solvate.

10